REMARKS

I. Status of the Application

Claims 23-43 were filed in the original application. In the Response to Office Action mailed March 17, 2006 claims 23 and 30 were amended, claims 28-29 and 35-43 were cancelled, and claims 44- 55 were added. In the Response to Final Office Action mailed July 6, 2006 claim 30 was amended, and claims 23-27 and 44-49 were cancelled. In the present Amendment and Response to Final Office Action of April 20, 2007, claims 30-33, and 50-54 are amended, claim 34 is cancelled, and claims 56- 62 are added. Therefore, claims 30-33, and 50-62 are currently pending.

The Applicants submit that the present amendments to the claims, and new claims, add no new subject matter. With regard to independent claim 30, support for the amendment "contacting nucleic acid from said virus with at least one pair of primers which hybridize to flanking sequences of said nucleic acid, wherein said flanking sequences flank a variable nucleic acid sequence of said virus;" may be found throughout the Specification at, for example, paragraph [0211]:

> [0211] In accordance with the present invention an approach of broad PCR priming across several different viral species is employed using conserved regions in the various viral genomes, amplifying a small, yet highly informative region in these organisms, and then analyzing the resultant amplicons with mass spectrometry and data analysis.

Support for "mass spectrometry" may be found throughout the Specification, and in the originally filed claims at, for example, paragraph [0211] and original claim 34.

Support for "comparing said base composition of said amplification product to calculated or measured base compositions of analogous amplification products of one or more known viruses present in a database comprising 5 or more base compositions." may be found throughout the Specification at, for example, paragraph [0063]:

[0063] FIG. 27 shows a representative base composition distribution of poxviruses for a single primer pair region on the DNA-dependent polymerase B gene (DdDpB). The spheres represent different poxvirus sequences that were used for primer design.

And paragraph [0209]:

[0209] As illustrated in FIG. 27, members of the Orthopoxvirus genus group can be identified, distinguished from one another, and distinguished from other members of the Poxvirus family using a single pair of primers designed against the DdRpB gene.

And paragraph [0210]:

[0210] Since the primers were designed across regions of high conservation within this genus, the likelihood of missed detection due to sequence variations at these sites is minimized. Further, none of the primers is expected to amplify other viruses or any other DNA, based on the data available in GenBank. This method can be used for all families of viral threat agents and is not limited to members of the Orthopoxvirus genus.

Accordingly, Figure 27. provides express support for a database comprising a plurality of base compositions corresponding to 5 or more viral species, for example, Variola virus, Monkeypox virus, Camelpox virus, Cowpox virus and Vaccinia virus.

Support for the element "with the proviso that sequencing of said amplification product is not used to identify the virus." may be found throughout the Specification at, for example, paragraph [0030]:

> [0030] Thus, there is a need for a method for bioagent detection and identification which is both specific and rapid, and in which no nucleic acid sequencing is required. The present invention addresses this need.

Dependent claims 31-33 are amended to correct typographic errors *i.e.*, "Claim" is amended to "claim". Dependent claim 31 is further amended to recite the "contacting" and "determining" steps of independent claim 30, and to delete the "measuring" step that is deleted herein from claim 30.

Dependent claims 50-55 are amended to correct punctuation by adding a comma *i.e.*, "claim 30**,** . . .". Dependent claim 54 is amended to correct its basis from independent claim 30 to new dependent claim 56.

The Applicants submit that the present additions to the claims add no new subject matter. With regard to new dependent claim 56, support may be found throughout the Specification at, for example, paragraph [0146]:

> [0146] RNA viruses cluster into families that have conserved RNA structural domains on the viral genome (e.g., virion components, accessory proteins) and conserved housekeeping genes that encode core viral proteins including, for single strand positive strand RNA viruses, RNA-dependent RNA polymerase, double stranded RNA helicase, chymotrypsin-like and papain-like proteases and methyltransferases. "Housekeeping genes" refers to genes that are generally always expressed and thought to be involved in routine cellular metabolism.

With regard to new dependent claim 57, support may be found throughout the Specification at, for example, paragraph [0089]:

> [0089] The triangulation identification process can be pursued by characterization of bioagent identifying amplicons in a massively parallel fashion using the polymerase chain reaction (PCR), such as multiplex PCR, and mass spectrometric (MS) methods.

With regard to new dependent claim 58, support may be found throughout the Specification at, for example, paragraph [0073]:

> [0073] These databases have been analyzed to determine regions that are useful as bioagent identifying amplicons. The characteristics of such regions include: a) between about 80 and 100%, or greater than about 95% identity among species of the particular bioagent of interest, of upstream and downstream nucleotide sequences which serve as sequence amplification primer sites; b) an intervening variable region which exhibits no greater than about 5% identity among species; and c) a separation of between about 30 and 1000 nucleotides, or no more than about 50-250 nucleotides, or no more than about 60-100 nucleotides, between the conserved regions.

With regard to new dependent claim 59, support may be found throughout the Specification at, for example, Figure 27.

With regard to new dependent claim 60, support may be found throughout the Specification at, for example, paragraph [0084]:

> [0084] In another embodiment of the invention, to compensate for the somewhat weaker binding by the "wobble" base, the oligonucleotide primers are designed such that the first and second positions of each triplet are occupied by nucleotide analogs which bind with greater affinity than the unmodified nucleotide.

With regard to new dependent claim 61, support may be found throughout the Specification at, for example, paragraph [0083]:

> [0083] For example, under this "wobble" pairing, inosine (I) binds to U, C or A; guanine (G) binds to U or C, and uridine (U) binds to U or C.

And paragraph [0084]:

> [0084] Examples of these analogs include, but are not limited to, 2,6-diaminopurine which binds to thymine, propyne T which binds to adenine and propyne C and phenoxazines, including G-clamp, which binds to G.

With regard to new dependent claim 62, support may be found throughout the Specification at, for example, paragraph [0101:

> [0101] If there are two or more targets of similar molecular mass, or if a single amplification reaction results in a product which has the same mass as two or more bioagent reference standards, they can be distinguished by using mass-modifying "tags."

The Applicants note that all amendments and cancellations of claims are made without acquiescing to any of the Examiner's arguments or rejections, and solely for the purpose of expediting the patent application process in a manner consistent with the PTO's Patent Business Goals (PBG),[1] and without waiving the right to prosecute the amended or cancelled claims (or similar claims) in the future.

In the Final Office Action of April 20, 2007 there are 2 rejections. The currently pending objection and rejections are:

1. Claims 30-34 and 50-54 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Jurinke et al (Genetic Analysis: Biomolecular Engineering (1996) 13:67-71) (hereinafter "Jurinke") in view of Norder et al (J Med Virol. (1990) 31:215-221) (herinafter "Norder") and further in view of Koster (WO 98/20166) (hereinafter "Koster").

1 65 Fed. Reg. 54603 (Sept. 8, 2000).

2. Claim 55 is rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Jurinke in view of Norder and further in view of Koster and further in view of Vanderhallen (J. Clin. Microbiol. (1998) 36(12):3463-3467) (hereinafter "Vanderhallen").

II. Rejections Under 35 U.S.C. 103(a)

A *prima facie* case of obviousness requires the Examiner to cite to a reference which a) discloses all the elements of the claimed invention, b) suggests or motivates one of ordinary skill in the art to combine the claim elements to yield the claimed invention, and c) provides a reasonable expectation of success should the claimed combination be carried out. Failure to establish any one of these three requirements negates a finding of a *prima facie* case and, without more, entitles the Applicants to allowance of the claims in issue. (MPEP)

In the Final Office Action of April 20, 2007 the Examiner notes:

> "Further, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize the viral targets and mass spectrometry method of Koster in the analytical method of Jurinke in view of Norder since Koster states "In another embodiment, an accurate **sequence determination** of a relatively large target nucleic acid can be obtained by generating specifically terminated fragments from the target nucleic acid, determining the mass of each fragment by mass spectrometry and ordering the fragments **to determine the sequence** of the larger nucleic acid (see page 75, line 26 to page 76, line 2)." So an ordinary practitioner would have been motivated to detect the PCR products of Jurinke in view of Norder with base composition Mass spectrometric approach of Koster since Koster teaches that Mass Spectrometry is accurate and can improve speed, mass accuracy and precision of the analysis. (see

abstract, for example)." (Final Office Action of April 20, 2007, page 6.) (Emphasis added)

The Applicants respectfully disagree. The Examiner's combinations of references fail to teach or suggest all elements of the presently claimed invention. For example, Jurinke in view of Norder and further in view of Koster, or Jurinke in view of Norder and further in view of Koster and further in view of Vanderhallen, fail to teach or suggest the element "sequencing of said amplification product is not used to identify the virus."

Moreover, the Applicants submit that there is no motivation to combine the cited references in the manner suggested by the Final Office Action of April 20, 2007, and, even if combined, there would be no expectation of success. To advance prosecution of the present application, in the Response to Final Office Action of July 6, 2006 the Applicants have presented a Declaration under 35 C.F.R. §1.132 by Dr. Steven Buchsbaum, a former Program Manager for the Defense Advanced Research Projects Agency (DARPA). In the Declaration, Dr. Buchsbaum notes the unexpected success of the methods described in the claims (see paragraph 3), the successful funding of a long-felt need (see paragraph 4), as well as provides independent commentaries and high visibility publications regarding the claimed technology (see paragraphs 5-10 and corresponding exhibits).

In view of the amendments to the claims and the accompanying Declaration, the Applicants respectfully submit that the claims are in condition for allowance.

CONCLUSION

All grounds of rejection of the Final Office Action dated April 20, 2007, have been addressed, and reconsideration of the application is respectfully requested. It is respectfully submitted that the Applicant's claims should be passed into allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicants encourage the Examiner to call the undersigned collect at (608) 218-6900.

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